

REMARKS

Favorable reconsideration, reexamination, and allowance of the present patent application are respectfully requested in view of the foregoing amendments and the following remarks. The foregoing amendments are fully supported by at least the original claims, and in the specification at page 13, 2nd full paragraph, page 14, 2nd full paragraph, and page 15, 3rd full paragraph. No new matter is entered by these amendments.

Objection to the Claims

At page 3 of the Office Action, Claim 1 was objected to because it allegedly contained informalities. Applicants respectfully requests reconsideration of this objection. Although Applicants do not necessarily agree with the interpretation of claim 1 as set forth in the Office Action, the claim has been amended as suggested by the Examiner. For at least the foregoing reasons, Applicants respectfully submit that Claim 1 is not objectionable, and therefore respectfully request withdrawal of the objection thereto.

Rejection under 35 U.S.C. § 112, second paragraph

In the Office Action, beginning at page 4, Claims 1-3, 6, 7 and 10 were rejected under 35 U.S.C. § 112, second paragraph, as reciting subject matters that allegedly are indefinite. Applicants respectfully request reconsideration of this rejection.

Regarding the rejection of claims 1-3 for reciting the relative terms “high” and “low”, Applicants have removed these terms from the claims, without prejudice.

Regarding the rejection of claim 1 for recitation of the phrase “mutant strain or genetic recombinant strain”, Applicants have removed this phrase from the claim, without prejudice.

For at least the foregoing reasons, Applicants respectfully submit that Claims 1-3,

6, 7 and 10 fully comply with 35 U.S.C. § 112, second paragraph, and therefore respectfully request withdrawal of the rejection thereof under 35 U.S.C. § 112.

Rejection under 35 U.S.C. § 112, first paragraph

In the Office Action, beginning at page 4, Claims 1-3, 6, 7 and 10 were rejected under 35 U.S.C. § 112, first paragraph, as the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with the claims. Applicants respectfully request reconsideration of this rejection.

Claim 1 has been amended to incorporate the limitations of claims 2 and 3, which should address many of the objections raised in the Office Action concerning the methods for enhancing enzyme activity and/or making an activity deficient in a cell (see pages 6, 11, and 13 of the Office Action). Furthermore, claim 1 has been amended to recite that the method involves culturing an *Escherichia coli* strain, which should address the objections in the Office Action regarding the unpredictability of culturing of any microorganism (see pages 6-8, 12-13 of the Office Action). Even further, claim 1 has been amended to recite that the enzyme activities to be enhanced are one of cytochrome bo-type oxidase and NDH-1, and those to be made deficient are cytochrome bd-type oxidase and NDH-II, which should address the objections in the Office Action regarding the ability of the skilled art worker to identify genes other than those that encode NDH-I, NDH-II, cytochrome bd, and cytochrome bo which will effect the energy efficiency of the cell (see page 12 of the Office Action).

As a result of these amendments, it is asserted that all of the bases for the rejection have been addressed. Specifically, the claims recite a method for producing a target substance using an *E. coli* strain which has the ability to produce said substance, and has been modified to either enhance the activity of cytochrome bo-type oxidase or NDH-I by increasing the copy number of a gene encoding the enzyme or by modifying

an expression regulatory sequence of said gene, and/or by making deficient the activity of cytochrome bd type oxidase or NDH-II by disrupting a gene coding this enzyme.

Therefore, when considering the teachings in the specification combined with the knowledge in the art concerning the recited enzymes and manipulation thereof in bacteria, it is clear that one of skill in the art could successfully practice the without undue experimentation.

For at least the foregoing reasons, Applicant respectfully submits that Claims 1-3, 6, 7 and 10 fully comply with 35 U.S.C. § 112, first paragraph, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 112.

In the Office Action, beginning at page 13, Claims 1, 6, 7 and 10 were rejected under 35 U.S.C. § 112, first paragraph, as reciting subject matters that allegedly is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant respectfully requests reconsideration of this rejection.

The amendments made to the claims, recited above, fully address all of the bases for this rejection as set forth in the Office Action. Specifically, the phrase “mutant or genetic recombinant” has been removed (see page 13 of the Office Action), the methods for enhancing enzyme activity or rendering it deficient are specified (see pages 14-15 of the Office Action), the relative terms “high” and “low” have been removed (see page 15 of the Office Action), and the strain has been amended to specify *E. coli* (see pages 15-16). Furthermore, although the genus of the enzymes’ activities to be enhanced or rendered deficient has been focused via the amendments, Applicants assert that the exemplified species of enhancing cytochrome bo oxidase and/or making deficient the activity of NDH-II are sufficient to adequately describe the genus, especially considering the genus of enzymes’ activities which are enhanced includes only one highly related additional species other than the exemplified species, and the genus of enzymes’

activities which are made deficient also includes only one highly related additional species other than the exemplified species. It is asserted that sufficient information is present in the prior art (see pages 8-9 the Office Action), combined with the description in the specification and exemplified species, to demonstrate that Applicants were in possession of the invention at the time of filing of the instant application.

For at least the foregoing reasons, Applicant respectfully submits that Claims 1, 6, 7 and 10 fully comply with 35 U.S.C. § 112, first paragraph, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 112.

Rejection under 35 U.S.C. § 102

In the Office Action, beginning at page 16, Claims 1-3, 7 and 10 were rejected under 35 U.S.C. § 102(b), as reciting subject matters that allegedly are anticipated by Ciccognani *et al.* Applicants respectfully request reconsideration of this rejection.

The claims recite that the produced target substance is collected from the medium in which the *E. coli* is cultured, and that the *E. coli* has the ability to produce and accumulate the target substance in the medium. The strain taught by Ciccognani *et al.* does not produce and accumulate the target substance in the culture medium, and therefore, the target substance cannot be collected from the medium.

The Office Action asserts on pages 18-19 that the claims recite no steps which are distinguishable from Ciccognani *et al.*; however, it is unclear where in Ciccognani *et al.* there is taught collection of the produced target substance. The claims recite that the target substance is collected from the medium in which the cells are cultured, and further that the cells have an ability to produce and accumulate said target substance in the medium. Such positive methods steps clearly distinguish the claims over the teachings of Ciccognani *et al.*, which clearly does not teach or suggest any excretion of any target substance into the medium, let alone the collection of any such substance.

For at least the foregoing reasons, Applicants respectfully submit that the subject

matters of Claims 1-3, 7 and 10 are not anticipated by Ciccognani *et al.*, are therefore not unpatentable under 35 U.S.C. § 102, and therefore respectfully request withdrawal of the rejection thereof under 35 U.S.C. § 102.

In the Office Action, beginning at page 17, Claims 1, 2, 7 and 10 were rejected under 35 U.S.C. § 102, as reciting subject matters that allegedly are anticipated by Spehr *et al.* Applicants respectfully request reconsideration of this rejection.

The method of claim 1 recites that the produced target substance is collected from the medium in which the *E. coli* is cultured, and that the *E. coli* has the ability to produce and accumulate the target substance in the medium in which it is cultured. Similar to above, the strain taught by Spehr *et al.* does not produce and accumulate the target substance in the culture medium, and therefore, the target substance cannot be collected from the medium.

For at least the foregoing reasons, Applicant respectfully submits that the subject matters of Claims 1, 2, 7 and 10 are not anticipated by Spehr *et al.*, are therefore not unpatentable under 35 U.S.C. § 102, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 102.

In the Office Action, beginning on page 18, a Response to Argument is presented. Specifically, on page 19 it is asserted that methods for mutating or constructing microorganisms to cause excretion of amino acids outside of the cell are known, and that the instant invention “does not teach means of engineering the cells for active excretion”. The Office Action also asserts that normal growth and replication processes would naturally cause accumulation of target substances within the cell, and that “natural accumulation of the target substances outside of the cell would occur through cellular lysis or rupture or through native excretion pathways...”. This logic is confusing, since on the same page the Office Action, citing to several literature articles, states that “it

appears that native strains do not actively excrete target substances such as amino acids into the medium but require specific engineering steps to generate appropriate strains for accumulation of the substances in the medium.” Therefore, the Office Action seems to be unable to determine whether target substances are expected to be excreted in to the medium or not?

Regardless of the confusing logic of the Office Action, the strain used in the claimed method has an inherent ability to produce and accumulate target substances in the medium when such a strain has been cultured in the medium, and such an ability is not inherently or explicitly taught or suggested by the cited prior art. Such a distinguishing characteristic is sufficient to remove the cited prior art references, and as such, the claims are not unpatentable under 35 U.S.C. § 102. Therefore, Applicants respectfully request withdrawal of the rejection thereof under 35 U.S.C. § 102 over the cited prior art.


Conclusion

For at least the foregoing reasons, Applicant respectfully submits that the present patent application is in condition for allowance. An early indication of the allowability of the present patent application is therefore respectfully solicited.

If Examiner Marvich believes that a telephone conference with the undersigned would expedite passage of the present patent application to issue, she is invited to call on the number below.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the undersigned authorizes that any necessary fees be charged to our deposit account 50-2821.

Respectfully submitted,

By: 
Shelly Guest Cermak
Registration No. 39,571

U.S. P.T.O. Customer No. 38108
Cermak & Kenealy, LLP
515 E. Braddock Road, Suite B
Alexandria, VA 22314
703.778.6608

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